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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,065	LAUTT ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8-18,21-25 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *7,18 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6, 8-17, 21, 23-25 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment to claims in the response flied on 12/11/06 has been acknowledged.

Claims 6-18, 21-25 and 29-31 are pending.

Claims 7, 18 and 22 have been withdrawn from further consideration as being drawn to non-elected species.

Claims 6, 8-17, 21, 23, 24 (in part to the extent that it reads on non-insulin dependent diabetes), 25 and 29-31 are examined on the merit.

Response to Arguments

With respect to applicants argument (page 7, paragraph 1, of applicant's remarks filed 12/11/06) about claim 7, applicants point out that the primary reference cited only discloses N-acetylcysteine, which is not nitrosylated should not have been included in the rejection. The restriction requirement of 6/14/06 required species election and applicants made an election of N-acetylcysteine and SIN-1 as their species. As required, and as per the restriction, "Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, **and a listing of all claims readable thereon**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election", see MPEP 809.02(a). Applicants did not make such an identification of claims that would read on the elected species. During examination, claims were searched for the elected species. Claim 7 was inadvertently

included in the non-final rejection of 9/11/2006 but should have been withdrawn. Therefore, due to the foregoing discussion claim 7 is hereby withdrawn from further consideration as being drawn to non-elected species.

Any objections and rejections not specifically mentioned here is considered withdrawn.

Withdrawn Rejections

Claim Rejections - 35 USC § 112, Second Paragraph

Rejection of claims 11 and 30 under 35 U.S.C. 112, second paragraph has been withdrawn in view of applicant's amendments to claims.

Claim Rejections - 35 USC § 102

Rejection of claims 6-8, 29 and 30 under 35 U.S.C. 102(b), has been withdrawn in view of applicant's amendments to claims. However, claims have been rejected under 35 USC § 112, first paragraph under new matter (see below). If the claims are again amended to overcome the new matter rejection original claim rejections under 35 U.S.C. 102(b) will be reinstated.

Claim Rejections - 35 USC § 103

Rejection of claims 6-17, 21, 23-25 and 29-31 under 35 U.S.C. 103, has been withdrawn in view of applicant's amendments to claims. However, claims have been rejected under 35 USC § 112, first paragraph under new matter (see below). If the claims are again amended to

overcome the new matter rejection original claim rejections under 35 U.S.C. 103 will be reinstated.

New ground of rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 8-17, 21, 23-25 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The previously presented claim recites "A pharmaceutical composition comprising a hepatic glutathione increasing compound and a hepatic nitric oxide-increasing compound".

The amended claims recite "A pharmaceutical composition comprising a combination of a therapeutically effective amount for reducing insulin resistance of a hepatic glutathione increasing compound and a therapeutically effective amount for reducing insulin resistance of a hepatic nitric oxide-increasing compound".

Lack of Ipsis Verbis Support

As amended, the claims call for the administration of agents that will reduce insulin resistance as a result of hepatic glutathione increasing compound and hepatic NO increasing compound. The specification lacks any *Ipsis Verbis* support that would support for the claims as amended. The support for amendments as indicated by the applicants on page 9, lines 22-29 of the originally presented specification discloses, "Any suitable glutathione-increasing compound and any suitable NO-increasing compound may be employed. A glutathione-increasing or NO-increasing compound will be "suitable" if: (a) at the dose and method of administration to the mammalian patient, it is not acutely toxic, and does not result in chronic toxicity disproportionate to the therapeutic benefit derived from treatment; and (b) at the dose and method of administration to the mammalian patient, including the impact of a suitable dose of the other (GSH or NO) increasing compound, it reduces insulin resistance in the patient". The disclosure as stated here in this section of the specification, exemplify that any glutathione increasing compound and any NO increasing compound can be employed. Further, this section of the specification dwells on the dosage requirement for these agents that is not toxic but it reduces insulin resistance in a patient. However, the amended claims imply administration of therapeutically effective amount of "any agent" for reducing insulin resistance as a result of administering a hepatic glutathione increasing compound and "any agent" for reducing insulin resistance as a result of administering a hepatic NO increasing compound. The specification is limited to treatment of insulin resistance using administering glutathione increasing compound and NO increasing compounds (see page 9, lines 22-29). The specification is silent with respect to agents that reduce insulin resistance caused by glutathione and NO increasing compounds.

The claim as amended does not have disclosure support in the specification and hence constitute new matter.

The term, 'mixtures thereof' in claims 14 and 15 lacks support in the specification as originally filed. The specification discussing specific embodiments on page 9 and 10 (as specified by the applicant's for support for the amendments) do not recite the term 'mixtures thereof' to define the instant invention. Mixtures imply the presence of more than one glutathione increasing compounds with NO increasing compounds and vice versa. The specification supports for the use of one glutathione increasing compound and one NO increasing compound. There is no literal support for claims as recited, because the term 'mixtures thereof' do not appear neither at the specified location and nor elsewhere in the specification.

Lack of Implicit Support

It is acknowledged that there is, it should be noted, that exact terms need not be used *in haec verba* to satisfy the written description requirement of the first paragraph of 35 U.S.C. 112. Newly added claims or amendment can be supported by implicit, or inherent disclosure.

The claims as amended lacks implicit support in the specification to corroborate the claims as recited. The amended claim recites limitations that are contrary to originally claimed invention and lacks implicit support in the specification at the location specified by the applicant and elsewhere in the application. The specification at the cite specified by the applicant for support to the amendment discloses, "Any suitable glutathione-increasing compound and any suitable NO-increasing compound may be employed. A glutathione-increasing or NO- increasing

compound will be "suitable" if: (a) at the dose and method of administration to the mammalian patient, it is not acutely toxic, and does not result in chronic toxicity disproportionate to the therapeutic benefit derived from treatment; and (b) at the dose and method of administration to the mammalian patient, including the impact of a suitable dose of the other (GSH or NO) increasing compound, it reduces insulin resistance in the patient". The disclosure as stated here in this section of the specification, exemplify that any glutathione increasing compound and any NO increasing compound can be employed. Further, this section of the specification dwells on the dosage requirement for these agents that is not toxic but it reduces insulin resistance in a patient. As amended, the claims call for the administration of agents that will reduce insulin resistance as a result of hepatic glutathione increasing compound and hepatic NO increasing compound. The amended claims imply administration of therapeutically effective amount of "any agent" for reducing insulin resistance as a result of administering a hepatic glutathione increasing compound and "any agent" for reducing insulin resistance as a result of administering a hepatic NO increasing compound. The specification is limited to treatment of insulin resistance using administering glutathione increasing compound and NO increasing compounds (see page 9, lines 22-29). The specification is silent with respect to agents that reduce insulin resistance caused by glutathione and NO increasing compounds. The support provided in the specification is for administration of glutathione increasing and NO increasing compounds and not for agents that affect insulin resistance as a result of administering glutathione increasing and NO increasing compounds. The claim as amended does not have disclosure support in the specification and hence constitute new matter.

The specification lacks any implicit support that would support the terms 'mixtures

thereof' (claims 7, 14 and 15). Lines 1-11 on page 10 are drawn as, "In one embodiment of the invention, the glutathione-increasing compound and NO-increasing compound are preferentially targeted to the liver. Targeting to the liver can be accomplished through the use of any pharmaceutically acceptable liver targeting substance. For example, each compound can be bound to albumin for preferential delivery to liver; alternatively, the compounds may be incorporated into or encapsulated within liposomes, which are preferentially targeted to the liver. Compounds can be bound to bile salts, which are selectively taken up by the liver. In one embodiment, one or both compounds are administered in a precursor form, and the precursor is selected to be metabolized to the active form by enzymes preferentially found in the liver". As seen here, there is lack of implicit support for the term 'mixtures thereof' in the specification at the location specified by the applicants and elsewhere in the application. Implicit support for the term "mixtures thereof" is lacking because only place where more than one compounds was mentioned was on page 10, line 9, that is drawn to "**one or both compounds**" in the alternative. Examples disclosed in the specification are limited to administering one glutathione increasing compound and one NO increasing compound. The term 'mixtures thereof' imply the presence of more than one glutathione increasing compounds with one NO increasing compounds and vice versa. The disclosure does not imply additional glutathione increasing compounds were administered with one NO increasing compound and vice versa. Therefore, claims as amended do not have implicit disclosure support in the specification and hence constitute new matter.

In conclusion, the specification does not provide reasonable support to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as amended.

Conclusion

Applicant's amendment to claims incorporating new matter into the claims as discussed above necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654

2/1/08
ANISH GUPTA
PRIMARY EXAMINER